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Cerebral Complications Incurred During Pregnancy and the Puerperium

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• In a statistical study of maternal mortality cases in Franklin County, Ohio, with a total of 170 deaths in a ten-year period (1948-1957), there were 36 fatal cases with cerebral complications of various types. Intracranial hemorrhage was the cause of death in 17 cases; subarachnoid hemorrhage in eight; intracerebral hemorrhage in eight and subdural hemorrhage in one case. There were nine cases of intracranial tumor with fatality. In a miscellaneous group of ten "cerebral deaths" infectious processes were the cause in eight cases, including tuberculous meningitis, purulent meningitis, brain abscess, acute (cerebromedullary) poliomyelitis, "viral" encephalitis, toxoplasmosis and tetanus.

In a smaller clinical (nonfatal) group with cerebral complications occurring during pregnancy and the puerperium, two patients with subarachnoid hemorrhages made spontaneous recovery. A diagnosis of intracerebral hemorrhage was made in three instances, in two of which operation was done and evacuation of blood clots was accomplished. One patient recovered spontaneously from a minimal hemorrhage.

Five other persons had cerebral thrombosis, three in the third month of pregnancy and two in the immediate puerperium. All recovered, with some residual deficits.

Three patients with intracranial tumor were successfully treated surgically but with disappointing results ultimately (one case each of cerebellar medulloblastoma, cerebral astrocytoma and supratentorial meningioma).

Only when the obstetrician, neurologist and the neurosurgeon are fully aware of the signs, symptoms, and many times the rapid course of these cerebral complications of pregnancy, can there be any material lowering of the morbidity and mortality. Emphasis should be placed on the early investigation of all neurological complaints during pregnancy and the puerperium, with immediate institution of an aggressive diagnostic and therapeutic regimen.

CEREBRAL COMPLICATIONS occurring during pregnancy and the puerperium has been the subject of several reviews in recent years that have emphasized such conditions as puerperal hemiplegia, subarachnoid and intracerebral hemorrhage, tumor and abscess, leptomeningeal and cerebral infectious processes, acute demyelinating diseases and other neurological disorders. From these reviews, it has been learned that all too frequently what appears to be minor symptoms and signs referable to the central nervous system are overlooked in pregnant patients or are thought of as "just expected to occur." Thus they are not given the attention they deserve until other more obvious or serious signs appear. As pointed out by Boshes and McBeath,[5] this neglect is particularly likely in the case of minor

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cerebral infarctions that may occur during pregnancy and the puerperium. Later the infarcted area gives rise to seizure activity and only then is the true nature of the original episode recognized. The serious significance of meningeal symptoms consequent to subarachnoid hemorrhage has been emphasized by Cannell and Botterell[6] and others.* This and other catastrophic intracranial lesions occurring during pregnancy and the puerperium are a challenge to neurosurgeons who ponder a reduction in the mortality and morbidity of these and other cerebral lesions. It seems worth while, therefore, to present a brief statistical analysis of fatal cases as well as a few examples of nonfatal cerebral complications personally observed.

MATERIAL

Obstetricians in Franklin County, Ohio, have a most active and discerning Maternal Mortality Study Committee which carefully reviews all cases of maternal deaths including those in which the patient died within the postpartum year. Through the courtesy and cooperation of this committee, the authors have been privileged to review and report here all deaths from 1948 through 1957 in which there were neurological complications or neurological conditions associated with pregnancy and the puerperium. In this ten-year period there were 157,654 live births and 170 maternal deaths; 36 of the maternal deaths (23 per cent) were of interest in this study (Table 1). So far as is known, there are no accurate statistics indicating the frequency of cerebral complications of nonfatal obstetrical cases. The authors, therefore, reviewed the records of all women 15 to 50 years of age in the University Hospital, Ohio State University, noting the occurrence of cerebrovascular accidents of all types and of intracranial tumors over the past ten-year period. To these have been added nonfatal clinical cases of cerebral complications of pregnancy taken from the personal files of one of us (not University Hospital cases). A total of 14 nonfatal cases was found that occurred during pregnancy and the puerperium (six months). It was soon apparent that not all cases with minor cerebral complications had been indexed and that those cases of cerebral vascular accidents occurring in the puerperium were not well cross-indexed. There will be presented, therefore, only a few examples of subarachnoid hemorrhage, puerperal hemiplegia, and intracranial tumors to emphasize the importance of thinking of these conditions when any neurological sign or symptom appears in pregnancy and the puerperium.

For this study, the records of the Franklin County Maternal Mortality Study Committee were used, taking all cases in which death occurred during pregnancy or within a six-month postpartum period. These cases were divided into the following groups: Subarachnoid hemorrhage, subdural hemorrhage, intracerebral hemorrhage, intracranial tumors, and a miscellaneous group of infectious processes, head injury, etc. (Table 2).

TABLE 1.—*Franklin County (Ohio) Maternal Mortality Study—10 Years, 1948-1957*

Total live births	157,654
Total deaths	170
Deaths due to central nervous system lesions	36

TABLE 2.—*Franklin County (Ohio) Maternal Mortality Study—10 Years, 1948-1957*

Intracranial causes of death:	
Intracranial tumors	9
Intracerebral hemorrhage	8
Subarachnoid hemorrhage	8
Viral or bacterial disease	8
Miscellany	3

Subarachnoid Hemorrhage

There were eight persons who died of subarachnoid hemorrhage during or shortly after pregnancy in this ten-year period from 1948 to 1957 inclusive (Table 3). The ages ranged from 22 to 42 (three each in the 20's and 30's and two in the 40's—41 and 42 years old respectively). Six of these persons had delivery at term; in one of the two the hemorrhage occurred at the eighth week and in the other in the thirty-second week of gestation. As to the six with delivery at term, one apparently had severe bleeding before going into labor and was soon comatose. Delivery was carried out with the patient in a respirator and she died two days later. In two other cases bleeding occurred about three hours postpartum, and in one each it had taken place on the third, sixth, and thirtieth postpartum day. Twins were born to one patient whose symptoms appeared about three hours postpartum. Six of these patients had had one or more previous pregnancies with a maximum of five. In the last instance there had been one abortion and four term pregnancies without previous signs of intracranial bleeding. None of these persons lived over six days after the clinical onset of subarachnoid hemorrhage. In four of the eight fatal cases death occurred within 24 hours; one patient was dead on arrival at the hospital, having lived only "a few minutes," and two each lived three days and six days respectively.

It is of some interest that one (without previous pregnancies) had had an acute subarachnoid hemorrhage 18 months before, and bilateral carotid angiography and ventriculography at that time showed no abnormalities. Unfortunately the vertebral-basilar arterial system had not been visualized

*References 8, 9, 11-18, 20-22, 24-26, 28, 29.

TABLE 3.—*Subarachnoid Hemorrhage, Franklin County (Ohio) Maternal Mortality Study—1948-1957 Inclusive*

Case	Age	Previous Pregnancies	Onset: Stage of Pregnancy	Period of Survival	Delivered	Previous S.A.H.	Diagnosis	Comments
1	22	0	8 weeks	6 days	No	0	S.A.H.	Negative angio. and ventric. No autopsy.
2	31	3	Term and 3 P.P.D.	1 day	Yes	0	S.A.H.	L.P., no other tests. No autopsy.
3	32	4	Term and a few hours	6 days	Yes. Twins	0	S.A.H., carotid aneurysm	L.P., angio., cranio. Clipped aneurysm. Autopsy.
4	27	0	Term—3 days	3 days ante- and 1 P.P.D.	Yes after S.A.H.	18 mo. previous	S.A.H.	L.P. negative angio. 18 mos. previous. Autopsy.
5	42	5	32 weeks	5 hours	Cesarean section	0	S.A.H.	L.P. only
6	32	2	Term and 3 hours	3 days	Yes	0	S.A.H.	L.P. only
7	41	1	Term and 1 day	1 day	Yes. 1 day S.A.H. in respirator	0	S.A.H.	L.P. only
8	24	5 (1 abortion, 4 term)	Term and 30 days	Few hours		0	S.A.H. aneurysm R.I.C.	Dead on arrival at hospital. Autopsy.

Abbreviations:
S.A.H. = Subarachnoid hemorrhage
L.P. = Lumbar puncture
R.I.C. = Right internal carotid
Angio. = Angiography
Ventric. = Ventriculography
Cranio. = Craniotomy
P.P.D. = Postpartum days

TABLE 4.—*Intracerebral Hemorrhage, Franklin County (Ohio) Maternal Mortality Study*

Case	Age	Onset: Gestation	Onset: Postpartum	Lived	Operation	Autopsy	Location of Hemorrhage
9	29	Term	Undelivered	14 days	.....	Yes	Intracerebral*
10	32	Term	Undelivered	18 hours	.....	Yes	Intracerebral†
11	20	6 months	Undelivered	12 hours	Yes	Yes	Intracranial, right frontal lobe‡
12	40	Term	1 day	14 days	Yes	Yes	Intracerebral, right frontal lobe
13	34	Term	.....	.....	.....	Yes	Intrapontine and slight subarachnoid
14	40	Term	2 hours	14 hours	.....	Yes	Intrapontine
15	22	4-5 months	Undelivered	8 hours	.....	Yes	Intrapontine
36	36	7 days postpartum	7 days postpartum	13 hours	Yes	Yes	Right parietotemporal

*Eclampsia. †Pre-eclampsia. ‡Also, necrosis of hypophysis.

nor had an interval angiographic study been performed when arterial spasm might have been absent and permitted a more accurate vascular survey.

The patient who died on the sixth posthemorrhage day was found to have a single aneurysm which was visualized angiographically and clipped intracranially. It may be that in that case the interval from the onset of the hemorrhage at 11 hours postpartum to the third postpartum day when angiography was performed was too long, although usually not considered to be so. This incident occurred before hypothermia was being used in Franklin County Hospitals.

The symptoms and signs of subarachnoid hemorrhage in the present series in no way deviated from those observed in other patients—headache and head pains, nausea, vomiting, stiffness of the neck, hemiplegia (in three cases) and bloody cerebrospinal fluid disclosed by lumbar puncture. It is unfortunate that more of the patients were not studied both by angiography and autopsy. In the absence of either diagnostic measure it may be presumed that in all cases the subarachnoid hemorrhages were due to rupture of an intracranial aneurysm in the circle of Willis or its immediate branches. Of course, this conclusion may or may not be correct in view of the known bleeding tendencies during pregnancy. If this assumption is true, however, it would appear

TABLE 5.—*Intracranial Tumors, Franklin County (Ohio) Maternal Mortality Study—10 Years, 1948-1957*

Case	Age	Onset	Diagnosis	Course and Procedures
17	23	1 hour postpartum	Parietal cystic glioma	One general seizure with rapid progression (2 hours) to coma and death
18	15	7½ months pregnancy	Intraventricular glioblastoma	H.A. progressed P.P., cranio. 15th P.P.D., death 15th P.O.D.
19	21	3 weeks postpartum	Parietal cystic astrocytoma	H.A., N. and V., L.P. and N.E. negative 5 days P.P., 19 days P.P. general seizures and apnea—death 24 hours later.
33	17	1 month of pregnancy	Temporal astrocytoma grade IV	N. and V. 1st month, right hemiparesis 1 month prepartum, hemiplegia by 3 weeks P.P., P.E.G. and cranio. Death 1 day postoperative.
34	28	1st month of pregnancy	Temporal astrocytoma grade II	Pre-eclampsia, dead fetus with induced labor. H.A. 2 weeks, cranio. with multiple re-exploration for wound infection.
16	29	5½ months postpartum	Occipital meningioma	Blurred vision 2 days then marked lethargy, aspiration, pneumonia with immediate death.
20	28	6 weeks postpartum	Malignant meningioma temporal lobe with massive hemorrhage	Sudden H.A. followed quickly by coma; cranio. done, death in 24 hours.
21	22	32 weeks pregnancy	Malignant ependymoma fourth ventricle	H.A., blurred vision and vertigo, diagnosis made, cesarean section and 12 days later cranio. Death 36 hours postoperative.
35	23	Immediate postpartum	Malignant fourth ventricle papilloma	1947 "burr holes" for pseudo tumor, P.P. H.A., blurred vision, diplopia, 50 days P.P. cranio. and ventcisternal shunt. Death 107 days P.P.

Abbreviations:
H.A.=Headache
N. and V.=Nausea and vomiting
L.P.=Lumbar puncture
P.E.G.=Pneumoencephalogram
N.E.=Neurological examination
P.O.D.=Postoperative day
P.P.D.=Postpartum day
P.P.=Postpartum
Cranio.=Craniotomy

that subarachnoid hemorrhage in the obstetrical period is peculiarly lethal.

Intracerebral Hemorrhage

Data regarding the eight fatal cases of cerebral hemorrhage are shown in Table 4. It will be noted that there were three patients each in the third and fourth decades of life and two in the fifth (each 40 years old). In three instances of intracerebral hemorrhage, eclampsia or preeclampsia were associated factors; in one of these there was necrosis of the hypophysis. Operative drainage of intracortical blood clots was accomplished in the two noneclamptic cases, and in one eclamptic case. It seems doubtful that anything could have been done surgically for the three patients with intrapontine (brain stem) hemorrhages.

The symptoms in this group were headache, convulsion, hemiplegia and coma—as well as the preexisting and apparently causative arterial hypertension in both the eclamptic and noneclamptic cases. The course of illness was cataclysmic, being rapidly fatal except in two cases with a survival of 14 days each.

The precise cause of the intracerebral hemorrhage was not always ascertained, although in one instance a small vascular malformation was observed at the margin of a massive hemorrhage into a frontal lobe. In a review of this problem, Christensen[7] concluded that massive intracerebral hemorrhage occurs only consequent to alterations of vascular walls—a condition which may exist during pregnancy and the puerperium. She also pointed out that such hemorrhages (subarachnoid, intracerebral, intraventricular) frequently arise in intracerebral and intramedullary vascular malformations.

Subdural Hematoma

Subdural bleeding occurred in only one instance, in that of a nurse who in the immediate puerperium had thrombophlebitis in one lower extremity and was treated with anticoagulants (heparin and bishydroxycoumarin). She was very ill and had shown signs of probable pulmonary embolism for which anticoagulants seemed justifiable. Nevertheless, subdural bleeding developed and was not recognized until the patient became comatose. The pupils of her eyes soon became dilated and fixed and respiratory failure followed. Neurosurgical intervention was obviously then too late.

Intracranial Neoplasms

Intracranial tumors were the cause of death in nine instances (Table 5).* There were three examples of astrocytoma (two cystic), two of glioblastoma multiforme (astrocytoma Grade IV), two of meningioma (one malignant), and one each of ep-

*In addition to these the authors have personal records of two more fatal cases, one of astroblastoma and the other of a low grade astrocytoma.

TABLE 6.—*Viral and Bacterial Disease, Franklin County (Ohio) Maternal Mortality Study*

Case	Age	Onset	Diagnosis	Survival
22	16	24 weeks pregnant	Tuberculous meningitis	1 month
22a	27	4½ months pregnant	Tuberculous meningitis	12 days
24	29	5 days postpartum	Tetanus	7 days
26	38	31 weeks pregnant	Septicemia and meningitis	2 days
27	27	7 months pregnant	Cerebellar abscess from otitis media	15 days
28	37	17 days postpartum	Poliomyelitis	30 days
29	25	Term	Toxoplasmosis	41 days
30	20	26 weeks pregnant	Viral encephalitis	1 week

endymoma and malignant papilloma (both in the fourth ventricle). Two occurred in the second decades (ages 15 and 17) and seven in the third decade (21 to 29 years).

In four cases the symptoms were few and practically unnoticed during pregnancy, but once they appeared death soon followed. One of the patients died of aspirating vomitus the second day after the onset of headache and lethargy. This occurred five and a half months after a normal term pregnancy and delivery. Another patient went through pregnancy without a symptom, save for a few headaches, then three and a half weeks after delivery suddenly had headache and vomiting. The results of neurological examination and of lumbar puncture and cerebrospinal fluid examination were reported as negative. A convulsion occurred five days later followed by apnea and death in 24 hours. At autopsy a parietal cystic astrocytoma with midbrain hemorrhage was found. In another case in the sixth week postpartum a malignant meningioma, which had remained silent until then, provoked a massive intracerebral hemorrhage which rapidly brought on headache and coma. Death followed in spite of prompt neurosurgical intervention. One patient had a generalized seizure one hour postpartum and died two hours later without any known previous symptoms. In five patients of this group, the onset of symptoms, of increased intracranial pressure or catastrophic manifestations occurred postpartum, one each, "immediately," one hour, three weeks, six weeks and five and a half months after parturition. In four cases symptoms occurred during pregnancy (one patient was delivered at seven and a half months) causing spontaneous delivery in one and surgical termination (cesarean section at 32 weeks) in another. In one, headaches, nausea and vomiting began after four weeks of gestation but the pregnancy went to term with spontaneous delivery. Operation was performed three weeks postpartum when she was hemiplegic and comatose and she died on the day of operation. Headaches were attributed to preeclampsia in one patient (Case 34, Table 5) and a dead fetus was removed by induced labor. Two weeks later a temporal lobe astrocytoma was resected. Death followed several months later from infection.

TABLE 7.—*Miscellaneous Neurological Causes of Death, Franklin County (Ohio) Maternal Mortality Study*

Case	Age	Onset	Diagnosis	Survival
25	39	3 months pregnant	Cerebral contusion	16 days
31	19	2 months pregnant	Guillain-Barré	11 days
32	25	38 days postpartum	Subdural hematoma	

Miscellaneous Group—Viral and Bacterial Infections

A group of women died each of diverse causes; data on them is summarized in Tables 6 and 7. These causes of death included infections (tuberculous meningitis, bacterial septicemia with meningitis, tetanus, cerebellar abscess, acute anterior poliomyelitis, toxoplasmosis, viral encephalitis), Guillain-Barré syndrome, anoxia (cardiac arrest) and trauma.

Nonfatal Cerebral Complications of Pregnancy And the Puerperium

Although many examples of neurological conditions present during pregnancy and the puerperium were studied, particular note was paid to only those who had apparent cerebral thrombosis, intracranial hemorrhages (subarachnoid, subdural and intracerebral bleeding) and intracranial tumors, since these conditions might lend themselves, in this present day, to some kind of definitive therapy. Pertinent data are given in Tables 8 to 11. It will be noted that there were not as many subarachnoid hemorrhages, intracerebral hemorrhages and tumors as in the fatal cases, which may be due to such factors as inadequate cross-indexing of records, the sometimes obscure nature of lesions and the tardiness in recognition of the symptoms. It should be emphasized that whereas cerebral thrombosis was not noted in the group of fatal cases, it occurred in four cases in the group of patients recovered (Table

TABLE 8.—*Subarachnoid Hemorrhage—Nonfatal Cases*

Case	Age	Previous Pregnancies	Onset: Stage of Pregnancy	Delivered	Previous Subarachnoid Hemorrhage	Diagnosis	Comments
1	38	0	8 hours postpartum	Yes	None	Subarachnoid hemorrhage	Complete angiogram negative; complete recovery
2	22	0	With labor	Yes	None	Subarachnoid hemorrhage and postcerebral thrombosis	Complete recovery

TABLE 9.—*Intracerebral Hemorrhage—Nonfatal Cases of Cerebral Complications of Pregnancy*

Case	Age	Onset	Previous Episodes	Complications	Diagnosis	Operations	Results
1	33	10 days P.P.	None	None	I.C.H. spontaneous	Angio., cranio., V.J. shunt	Hydroceph. blind
2	27	5 days P.P.	None	None	I.C.H. spontaneous	None	Recovery
3	27	With labor	None	None	A.-V. malformation	Angio., cranio.	Minimal hemiparesis

Abbreviations:
I.C.H. = Intracranial hemorrhage
Angio. = Angiography
Cranio. = Craniotomy
V.J. = Ventriculojugular
A.V. = Arteriovenous
P.P. = Postpartum

TABLE 10.—*Miscellaneous Nonfatal Cases of Cerebral Complications of Pregnancy*

Case	Age	Onset	Previous Episodes	Complications	Diagnosis	Operations	Results
1	27	3 months pregnant	None	None	Cerebral thrombosis	None	Hemiparesis
2	30	3-4 hours postpartum	None	Pre-eclampsia	C.V.A. hemorrhage	None	Hemiparesis
3	27	3 months pregnant	None	None	Thrombosis internal carotid	Angiography	Mild hemiparesis
4	21	3 months pregnant	None	None	Thrombosis middle cerebral artery	Angio. and sup. cer. S. ganglionectomy	Mild hemiparesis
5	39	6 days postpartum	None	None	Cerebral thrombosis	Angiography	Mild hemiparesis
6	29	5½ months pregnant	None	None	Trauma, skull fracture, subdural hematoma	Craniotomy	Personality changes, slight aphasia, hemiparesis

Abbreviations:
Angio. = Angiography
Sup. Cer. S. = Superior cervical sympathetic
C.V.A. = Cerebral vascular accident

10). This suggests, therefore, the need of adequate neurological investigation of all untoward symptoms during pregnancy and the puerperium referable to the brain, including ophthalmoscopic, x-ray and electroencephalographic examinations, and, when indicated, examination of the cerebrospinal fluid, and in some cases angiography and air studies. Only when these investigations are promptly carried out can one expect to arrive at early diagnosis and appropriate therapy, and thus reduce the mortality or improve the results in the nonfatal cases.

GENERAL CONSIDERATIONS

It would appear from this study and that of Cannell and Botterell[6] that subarachnoid hemorrhage is an extreme emergency and needs immediate neurosurgical attention. With the routine use of hypotension and hypothermia and possibly newer methods to come, it may be that it will be found that earlier surgical intervention will reduce the mortality in this group.

Earlier diagnosis and surgical removal of intracerebral blood clots are of equal importance, and it is believed that this will eventually produce much brighter results than those recorded here.

Cerebral thrombosis is a condition which occurs all too frequently during pregnancy. This problem has been emphasized by Martin,[19a] Martin and Sheehan,[19b] Symonds,[27] Boshes and McBeath,[5] Alpers and Palmer[1] and many others. It appears that not in all instances is this lesion due to primary arterial thrombosis. It may well represent (a) thrombosis of venous sinuses, or even (b) a retrograde embolism from the pelvic veins via the paravertebral veins of Batson[3] (Martin[19a]). This brings to light the problem of vascular wall and blood clotting changes that occur during pregnancy and the puerperium and may have a direct bearing on obstetric and puerperal thrombosis. Infection as a cause of

TABLE 11.—*Intracranial Tumors—Nonfatal Cases*

Case	Age	Onset	Diagnosis	Course and Procedure	Results
1	27	Labor	Cerebellar medulloblastoma	Headache and diplopia, after delivery ventriculography, subtotal excision	Poor course, downhill
2	20	4 months pregnant	Cerebellar astrocytoma grade II	Headache, lightheadedness, diplopia, vertigo, ataxia, ventriculography, craniotomy, ventriculocisternal shunt	Poor course, downhill
3	24	6 years intermittent	Sphenoidal ridge meningioma	Headache, blurred vision, no operation	No increase in symptoms, severity or frequency

cerebral venous thrombosis is not to be overlooked.

The danger in the use of anticoagulants for thrombophlebitis is well illustrated by the case in this series in which the use of bishydroxycoumarin resulted in spontaneous subdural hemorrhage that was unrecognized until coma occurred. Only then was the patient referred for neurosurgical care, too late to prevent a fatal issue. Earlier recognition of the neurological signs of clouding of the sensorium, mild hemiparesis and early papillary changes might have prevented death.

In patients with intracranial tumor a somewhat different problem is presented. Most investigators believe that the brain becomes edematous or in some way increased in volume during or immediately after pregnancy. This apparently is associated more with meningiomas[2,30] and acoustic neurofibromas[4] than with tumors of glial origin.[10,22,23,25] Angiomas become engorged and are subject to thrombosis and hemorrhage. If hemorrhage occurs in or around such a tumor, the symptoms may prove to be catastrophic, as in the case of a meningioma in the "fatal" series here reported. Otherwise, the onset of symptoms may appear more gradually, requiring close and accurate observation. When recognized, appropriate neurosurgical attention must follow in this group of cases. It is now also appreciated by most neurosurgeons that patients with tumors soon develop more cerebral edema and other complications than do the nonpregnant or nonpuerperal patients. This suggests the need for further studies on cerebral edema, cerebrovascular states and electrolytic balance in the obstetrical and puerperal periods.

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NOTE: An extensive review of the literature which was a part of this presentation when it was read, has been omitted from this published version.

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